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EXAMINER	
REDDIG, PETER J	
ART UNIT	PAPER NUMBER
1642	
MAIL DATE	DELIVERY MODE
01/22/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,485	MUNNES ET AL.	
	Examiner	Art Unit	
	Peter J. Reddig	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *1* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/16/2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-24* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group 1, claim(s) 1 and claims 5-10 and 16-18, in part, drawn to a method for characterizing the state of a neoplastic disease in a subject, comprising (i) determining the pattern of expression levels of at least 6,8, 10,15, 20,30, or 47 marker genes, comprised in a group of marker genes consisting of SEQ ID NO : 1 to 165, in a biological sample from said subject, (ii) comparing the pattern of expression levels determined in (i) with one or several reference pattern (s) of expression levels, (iii) characterizing the state of said neoplastic disease in said subject from the outcome of the comparison in step (ii)..

Group 2, claim(s) 2 and claims 5-10 and 16-18, in part, drawn to a method for characterizing the state of a neoplastic disease in a subject, comprising (i) determining the pattern of expression levels of at least 6,8, 10,15, 20,30, 47 or 67 marker genes, comprised in a group of marker genes consisting of SEQ ID NO : 1 to 165 and 472 to 491, in a biological sample from said subject, (ii) comparing the pattern of expression levels determined in (i) with one or several reference pattern (s) of expression levels, (iii) characterizing the state of said neoplastic disease in said subject from the outcome of the comparison in step (ii).

Group 3, claim(s) 3 and claims 5 and 16-18, in part, drawn to a method for detection, diagnosis, screening, monitoring, and/or prognosis of a neoplastic disease in a subject, comprising (i) determining the pattern of expression levels of at least 1, 2,3, 5,10, 15,20, 30, or 47 marker genes, comprised in a group of marker genes consisting of SEQ ID NOs : 1 to 17,19 to 33, 35 to 50, 52 to 64, 66 to 85,88 to 91, and 93 to 165 in biological samples from said subject, (ii) comparing the pattern of expression levels determined in (i) with one or several reference pattern (s) of expression levels, (iii) detecting, diagnosing, screening, monitoring, and/or prognosing said neoplastic disease in said subject from the outcome of the comparison in step (ii).

Group 4, claim(s) 4 and claims 5 and 16-18, in part,, drawn to a method for detection, diagnosis, screening, monitoring, and/or prognosis of a neoplastic disease in a subject, comprising (i) determining the pattern of expression levels of at least 1, 2, 3, 5, 10,15, 20,30, 47, or 67 marker genes, comprised in a group of marker genes consisting of SEQ ID NOs : 1 to 17, 19 to 33, 35 to 50, 52 to 64, 66 to 85, 88 to 91, and 93 to 165 and 472 to 491 in biological samples from said

subject, (ii) comparing the pattern of expression levels determined in (i) with one or several reference pattern (s) of expression levels, (iii) detecting, diagnosing, screening, monitoring, and/or prognosing said neoplastic disease in said subject from the outcome of the comparison in step (ii).

Claim 11 links inventions 5 and 6. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 11. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP ' 804.01.

Group 5, claim(s) 16-18, in part, drawn to a method of treatment for a subject afflicted with a neoplastic disease, comprising (i) identifying the most promising mode of treatment with the method of claim 6 or 7, (ii) treating said neoplastic disease in said patient by the mode of treatment identified in step (i) using the method of claim 1.

Group 6, claim(s) 16-18, in part, drawn to a method of treatment for a subject afflicted with a neoplastic disease, comprising (i) identifying the most promising mode of treatment with the method of claim 6 or 7, (ii) treating said neoplastic disease in said patient by the mode of treatment identified in step (i) using the method claim 2.

Claim 12 links inventions 7-10. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 12. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and

any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP ' 804.01.

Group 7, claim(s) 16-18, in part, drawn to a method of screening for subjects afflicted with a neoplastic disease, wherein a method of claim 1 is applied to a plurality of subjects.

Group 8, claim(s) 16-18, in part, drawn to a method of screening for subjects afflicted with a neoplastic disease, wherein a method of claim 2 is applied to a plurality of subjects.

Group 9, claim(s) 16-18, in part, drawn to a method of screening for subjects afflicted with a neoplastic disease, wherein a method of claim 3 is applied to a plurality of subjects.

Group 10, claim(s) 16-18, in part, drawn to a method of screening for subjects afflicted with a neoplastic disease, wherein a method of claim 4 is applied to a plurality of subjects.

Claim 13 links inventions 11 and 12. The restriction requirement among the linked inventions is subject to the nonallowance of the linking claim(s), claim 13. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable

linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP ' 804.01.

Group 11, claim(s) 16-18, in part, drawn to a method of screening for substances and/or therapy modalities having curative effect on a neoplastic disease comprising (i) obtaining a biological sample from a subject afflicted with said neoplastic disease, (ii) assessing, from said biological sample, using the method of claim 6 or 7, whether said subject is expected to respond to a given mode of treatment for said neoplastic disease, (iii) if said subject is expected to respond to said given mode of treatment, incubating said biological sample with said substance under said therapy modalities, (iv) observing changes in said biological sample triggered by said test substance under said therapy modalities, (v) selecting or rejecting said test substance and/or said therapy modalities, based on the observation of changes in said biological sample under (iv)using the method of claim 1.

Group 12, claim(s) 16-18, in part, drawn to a method of screening for substances and/or therapy modalities having curative effect on a neoplastic disease comprising (i) obtaining a biological sample from a subject afflicted with said neoplastic disease, (ii) assessing, from said biological sample, using the method of claim 6 or 7, whether said subject is expected to respond to a given mode of treatment for said neoplastic disease, (iii) if said subject is expected to respond to said given mode of treatment, incubating said biological sample with said substance under said therapy modalities, (iv) observing changes in said biological sample triggered by said test substance under said therapy modalities, (v) selecting or rejecting said test substance and/or said therapy modalities, based on the observation of changes in said biological sample under (iv) using the method claim 2.

Group 13, claim(s) 14 and claims 16-18, in part, drawn to a method of screening for compounds having curative effect on a neoplastic disease comprising (i) incubating biological samples or extracts of these with a test substance, (ii) determining the pattern of expression levels of at least 1,2, 3,5, 10,15, 20,30, or 47 marker genes, comprised in a group of marker genes consisting of SEQ ID NO : 1 to 17, 19 to 33, 35 to 50, 52 to 64, 66 to 85, 88 to 91, and 93 to 165 in said biological sample, (iii) comparing the pattern of expression levels determined in (ii) with one or several reference pattern (s), (iv) selecting or rejecting said test substance, based on the comparison performed under (iii).

Group 14, claim(s) 15 and claims 16-18, in part, drawn to a method of screening for compounds having curative effect on a neoplastic disease comprising (i) incubating biological samples or extracts of these with a test substance, (ii) determining the pattern of expression levels of at least

1,2, 3,5, 10,15, 20,30, 47, or 67 marker genes, comprised in a group of marker genes consisting of SEQ ID NO : 1 to 17, 19 to 33, 35 to 50, 52 to 64, 66 to 85, 88 to 91, and 93 to 165 and 472 to 491 in said biological sample, (iii) comparing the pattern of expression levels determined in (ii) with one or several reference pattern (s), (iv) selecting or rejecting said test substance, based on the comparison performed under (iii).

Group 15, claim(s) 19, drawn to a kit comprising at least 6, 8, 10,15, 20, 30, or 47 primer pairs and probes suitable for marker genes comprised in a group of marker genes consisting of (i) SEQ ID NO : 1 to SEQ ID NO : 165, or (iii) the marker genes listed in Table 2.

Group 16, claim(s) 20, drawn to a kit comprising at least 6, 8, 10, 15, 20, 30, 47, or 67 primer pairs and probes suitable for marker genes comprised in a group of marker genes consisting of (i) SEQ ID NO: 1 to SEQ ID NO: 165, and/or (ii) SEQ ID NO: 472 to SEQ ID NO: 491, or (iii) the marker genes listed in Table 2.

Group 17, claim(s) 21, drawn to a kit comprising at least 6, 8, 10,15, 20, 30, or 47 individually labeled probes, each having a sequence comprised in a group of sequences consisting of SEQ ID NO : 331 to SEQ ID NO : 471.

Group 18, claim(s) 22, drawn to a kit comprising at least 6, 8, 10,15, 20, 30, 47 or 67 individually labeled probes, each having a sequence comprised in a group of sequences consisting of SEQ ID NO : 331 to SEQ ID NO : 471 and SEQ ID NO : 512 to 571.

Group 19, claim(s) 23, drawn to a kit comprising at least 6, 8, 10,15, 20, 30, or 47 arrayed probes, each having a sequence comprised in a group of sequences consisting of SEQ ID NO : 331 to SEQ ID NO : 471.

Group 20, claim(s) 24, drawn to a kit comprising at least 6, 8, 10,15, 20, 30, 47 or 67 arrayed probes, each having a sequence comprised in a group of sequences consisting of SEQ ID NO : 331 to SEQ ID NO : 471 and SEQ ID NO : 512 to 571.

The inventions listed as Groups 1-20 do not relate to a single general inventive concept under PCT Rule 13.1 because unity of invention between different categories of inventions will only be found to exist if specific combinations of inventions are present. Those combinations include:

A) A product and a special process of manufacture of said product.

B) A product and a process of use of said product.

C) A product, a special process of manufacture of said product, and a process of use of said product.

D) A process and an apparatus specially designed to carry out said process.

E) A product, a special process of manufacture of said product, and an apparatus specially designed to carry out said process.

The inventions of groups 1-20 are drawn to multiple products as well as multiple methods of using those products. Allowed combinations do not include multiple products, and multiple methods of using said products, as claimed in the instant application. Hence, only one product and one process of use of said product relate to a single general inventive concept. Since multiple products and multiple methods with different special technical features are claimed, the first invention of the category first mentioned in the claims of the application will be considered as the main invention in the claims, see PCT article 17(3) (a) and 1.476 (c), 37 C.F.R. 1.475(d). Group 1 is drawn to a process of a product. Groups 2-16 are additional products and methods of using those products. Accordingly, Groups 1-20 are not so linked as to form a single general inventive concept and the finding of lack of unity is proper.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) **and (ii) identification of the claims encompassing the elected invention**.

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be

considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Species Elections for Group 1

A. Claim 1 is generic to the following patentably distinct species of markers: SEQ ID NO: 1-165. Applicants must elect a specific, defined combination of markers consistent with the limitations of the claims, e.g. SEQ ID NO: 1-6.

B. Claim 1 is generic to the following patentably distinct species of determining the expression level:

1) with a hybridization based method, or with a hybridization based method utilizing arrayed probes, or with a hybridization based method utilizing individually labeled probes, or by real time real time PCR,

2) by assessing the expression of polypeptides, proteins or derivatives thereof, or (vi) by assessing the amount of polypeptides, proteins or derivatives thereof.

Species Elections for Group 2

A. Claim 2 is generic to the following patentably distinct species of markers: SEQ ID NO: 1 to 165 and 472 to 491. Applicants must elect a specific, defined combination of markers consistent with the limitations of the claims, e.g. SEQ ID NO: 1-6.

B. Claim 2 is generic to the following patentably distinct species of determining the expression level:

1) with a hybridization based method, or with a hybridization based method utilizing arrayed probes, or with a hybridization based method utilizing individually labeled probes, or by real time real time PCR,

2) by assessing the expression of polypeptides, proteins or derivatives thereof, or (vi) by assessing the amount of polypeptides, proteins or derivatives thereof.

Species Elections for Group 3

A. Claim 3 is generic to the following patentably distinct species of markers: SEQ ID NO: 1 to 17, 19 to 33, 35 to 50, 52 to 64, 66 to 85, 88 to 91, and 93 to 165. Applicants must elect a specific, defined combination of markers consistent with the limitations of the claims, e.g. SEQ ID NO: 1 and 2.

B. Claim 3 is generic to the following patentably distinct species of determining the expression level:

1) with a hybridization based method, or with a hybridization based method utilizing arrayed probes, or with a hybridization based method utilizing individually labeled probes, or by real time real time PCR,

2) by assessing the expression of polypeptides, proteins or derivatives thereof, or (vi) by assessing the amount of polypeptides, proteins or derivatives thereof.

Species Elections for Group 4

A. Claim 4 is generic to the following patentably distinct species of markers: SEQ ID NO : 1 to 17, 19 to 33, 35 to 50, 52 to 64 ,66 to 85, 88 to 91, 93 to 165 and 472 to 491. Applicants must elect a specific, defined combination of markers consistent with the limitations of the claims, e.g. SEQ ID NO: 1 and 2.

B. Claim 4 is generic to the following patentably distinct species of determining the expression level:

1) with a hybridization based method, or with a hybridization based method utilizing arrayed probes, or with a hybridization based method utilizing individually labeled probes, or by real time real time PCR,

2) by assessing the expression of polypeptides, proteins or derivatives thereof, or (vi) by assessing the amount of polypeptides, proteins or derivatives thereof

Species Elections for Group 5

A. Claim 11 is generic to the following patentably distinct species of markers: SEQ ID NO: 1-165. Applicants must elect a specific, defined combination of markers consistent with the limitations of the claims, e.g. SEQ ID NO: 1-6.

B. Claim 11 is generic to the following patentably distinct species of determining the expression level:

1) with a hybridization based method, or with a hybridization based method utilizing arrayed probes, or with a hybridization based method utilizing individually labeled probes, or by real time real time PCR,

2) by assessing the expression of polypeptides, proteins or derivatives thereof, or (vi) by assessing the amount of polypeptides, proteins or derivatives thereof.

Species Elections for Group 6

A. Claim 11 is generic to the following patentably distinct species of markers: SEQ ID NO: 1 to 165 and 472 to 491. Applicants must elect a specific, defined combination of markers consistent with the limitations of the claims, e.g. SEQ ID NO: 1-6.

B. Claim 11 is generic to the following patentably distinct species of determining the expression level:

1) with a hybridization based method, or with a hybridization based method utilizing arrayed probes, or with a hybridization based method utilizing individually labeled probes, or by real time real time PCR,

2) by assessing the expression of polypeptides, proteins or derivatives thereof, or (vi) by assessing the amount of polypeptides, proteins or derivatives thereof.

Species Elections for Group 7

A. Claim 12 is generic to the following patentably distinct species of markers: SEQ ID NO: 1-165. Applicants must elect a specific, defined combination of markers consistent with the limitations of the claims, e.g. SEQ ID NO: 1-6.

B. Claim 12 is generic to the following patentably distinct species of determining the expression level:

1) with a hybridization based method, or with a hybridization based method utilizing arrayed probes, or with a hybridization based method utilizing individually labeled probes, or by real time real time PCR,

2) by assessing the expression of polypeptides, proteins or derivatives thereof, or (vi) by assessing the amount of polypeptides, proteins or derivatives thereof.

Species Elections for Group 8

A. Claim 12 is generic to the following patentably distinct species of markers: SEQ ID NO: 1 to 165 and 472 to 491. Applicants must elect a specific, defined combination of markers consistent with the limitations of the claims, e.g. SEQ ID NO: 1-6.

B. Claim 12 is generic to the following patentably distinct species of determining the expression level:

1) with a hybridization based method, or with a hybridization based method utilizing arrayed probes, or with a hybridization based method utilizing individually labeled probes, or by real time real time PCR,

2) by assessing the expression of polypeptides, proteins or derivatives thereof, or (vi) by assessing the amount of polypeptides, proteins or derivatives thereof.

Species Elections for Group 9

A. Claim 12 is generic to the following patentably distinct species of markers: SEQ ID NO: 1 to 17, 19 to 33, 35 to 50, 52 to 64 ,66 to 85, 88 to 91, and 93 to 165. Applicants must elect a specific, defined combination of markers consistent with the limitations of the claims, e.g. SEQ ID NO: 1 and 2.

B. Claim 12 is generic to the following patentably distinct species of determining the expression level:

1) with a hybridization based method, or with a hybridization based method utilizing arrayed probes, or with a hybridization based method utilizing individually labeled probes, or by real time real time PCR,

2) by assessing the expression of polypeptides, proteins or derivatives thereof, or (vi) by assessing the amount of polypeptides, proteins or derivatives thereof.

Species Elections for Group 10

A. Claim 12 is generic to the following patentably distinct species of markers: SEQ ID NO: 1 to 17, 19 to 33, 35 to 50, 52 to 64 ,66 to 85, 88 to 91, 93 to 165 and 472 to 491. Applicants must elect a specific, defined combination of markers consistent with the limitations of the claims, e.g. SEQ ID NO: 1 and 2.

B. Claim 12 is generic to the following patentably distinct species of determining the expression level:

1) with a hybridization based method, or with a hybridization based method utilizing arrayed probes, or with a hybridization based method utilizing individually labeled probes, or by real time real time PCR,

2) by assessing the expression of polypeptides, proteins or derivatives thereof, or (vi) by assessing the amount of polypeptides, proteins or derivatives thereof

Species Elections for Group 11

A. Claim 13 is generic to the following patentably distinct species of markers: SEQ ID NO: 1-165. Applicants must elect a specific, defined combination of markers consistent with the limitations of the claims, e.g. SEQ ID NO: 1-6.

B. Claim 13 is generic to the following patentably distinct species of determining the expression level:

1) with a hybridization based method, or with a hybridization based method utilizing arrayed probes, or with a hybridization based method utilizing individually labeled probes, or by real time real time PCR,

2) by assessing the expression of polypeptides, proteins or derivatives thereof, or (vi) by assessing the amount of polypeptides, proteins or derivatives thereof.

Species Elections for Group 12

A. Claim 13 is generic to the following patentably distinct species of markers: SEQ ID NO: 1 to 165 and 472 to 491. Applicants must elect a specific, defined combination of markers consistent with the limitations of the claims, e.g. SEQ ID NO: 1-6.

B. Claim 13 is generic to the following patentably distinct species of determining the expression level:

1) with a hybridization based method, or with a hybridization based method utilizing arrayed probes, or with a hybridization based method utilizing individually labeled probes, or by real time real time PCR,

2) by assessing the expression of polypeptides, proteins or derivatives thereof, or (vi) by assessing the amount of polypeptides, proteins or derivatives thereof.

Species Elections for Group 13

A. Claim 14 is generic to the following patentably distinct species of markers: SEQ ID NO : 1 to 17, 19 to 33, 35 to 50, 52 to 64 ,66 to 85, 88 to 91, and 93 to 165. Applicants must elect a specific, defined combination of markers consistent with the limitations of the claims, e.g. SEQ ID NO: 1 and 2.

B. Claim 14 is generic to the following patentably distinct species of determining the expression level:

1) with a hybridization based method, or with a hybridization based method utilizing arrayed probes, or with a hybridization based method utilizing individually labeled probes, or by real time real time PCR,

2) by assessing the expression of polypeptides, proteins or derivatives thereof, or (vi) by assessing the amount of polypeptides, proteins or derivatives thereof

Species Elections for Group 14

A. Claim 15 is generic to the following patentably distinct species of markers: SEQ ID NO: 1 to 17, 19 to 33, 35 to 50, 52 to 64 ,66 to 85, 88 to 91, 93 to 165 and 472 to 491. Applicants must elect a specific, defined combination of markers consistent with the limitations of the claims, e.g. SEQ ID NO: 1 and 2.

B. Claim 15 is generic to the following patentably distinct species of determining the expression level:

1) with a hybridization based method, or with a hybridization based method utilizing arrayed probes, or with a hybridization based method utilizing individually labeled probes, or by real time real time PCR,

2) by assessing the expression of polypeptides, proteins or derivatives thereof, or (vi) by assessing the amount of polypeptides, proteins or derivatives thereof

Species Elections for Group 15

A. Claim 19 is generic to the following patentably distinct species of marker genes: (i) SEQ ID NO: 1 to SEQ ID NO: 165, or (ii) the marker genes listed in Table 2. Applicants must elect a specific, defined combination of marker genes consistent with the limitations of the claims, e.g. SEQ ID NO: 1-6.

Species Elections for Group 16

A. Claim 20 is generic to the following patentably distinct species of marker genes: (i) SEQ ID NO: 1 to SEQ ID NO: 165, and/or (ii) SEQ ID NO: 472 to SEQ ID NO: 491, or (iii) the marker genes listed in Table 2. Applicants must elect a specific, defined combination of marker genes consistent with the limitations of the claims, e.g. SEQ ID NO: 1-6.

Species Elections for Group 17

A. Claim 21 is generic to the following patentably distinct species of sequences: SEQ ID NO: 331 to SEQ ID NO: 471. Applicants must elect a specific, defined combination of marker genes consistent with the limitations of the claims, e.g. SEQ ID NO: 331-337.

Species Elections for Group 18

A. Claim 22 is generic to the following patentably distinct species of sequences SEQ ID NO: 331 to SEQ ID NO: 471 and SEQ ID NO: 512 to 571. Applicants must elect a specific, defined combination of marker genes consistent with the limitations of the claims, e.g. SEQ ID NO: 331-337.

Species Elections for Group 19

A. Claim 23 is generic to the following patentably distinct species of sequences SEQ ID NO: 331 to SEQ ID NO: 471. Applicants must elect a specific, defined combination of marker genes consistent with the limitations of the claims, e.g. SEQ ID NO: 331-337.

Species Elections for Group 20

A. Claim 24 is generic to the following patentably distinct species of sequences SEQ ID NO: 331 to SEQ ID NO: 471 and SEQ ID NO: 512 to 571. Applicants must elect a specific, defined combination of marker genes consistent with the limitations of the claims, e.g. SEQ ID NO: 331-337.

The species are independent or distinct because as disclosed the different species have mutually exclusive characteristics for each identified species. In addition, these species are not obvious variants of each other based on the current record.

In accordance with the decisions in *In re Harnisch*, 631 F.2d 716, 206 USPQ 300 (CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984), restriction of a Markush group is proper where the compounds within the group either (1) do not share a common utility, or (2) do not share a substantial structural feature disclosed as being essential to that utility. In addition, a Markush group may encompass a plurality of independent and distinct inventions where two or more members are so unrelated and diverse that a prior art reference anticipating the claim with respect to one of the members would not render the other member(s) obvious under 35 USC 103. Since the decisions in *In re Weber*, 198 USPQ 328 (CCPA 1978) and *In re Hass*, 198 USPQ 334 (CCPA 1978), it is proper for the Office to refuse to examine that

which applicants regard as their invention, if the subject matter in a claim lacks unity of invention, see MPEP 803.02.

Further some of the species are related as combination and subcombination. Species in this relationship are distinct if it can be shown that (1) the patentability of the combination does not rely necessarily and solely on the patentability of any one subcombination and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the patentability of the combination does not rely necessarily and solely on the patentability of any one subcombination as clearly evidenced by the plural subcombinations claimed. Further, each of the subcombinations has utility by itself because each of the subcombinations is useful for screening for different variables and different markers. Thus the claims are distinct as required by MPEP 806.05(c).

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

There is an examination and search burden for these patentably distinct species due to their mutually exclusive characteristics. The species require a different field of search (e.g., searching different classes/subclasses or electronic resources, or employing different search queries); and/or the prior art applicable to one species would not likely be applicable to another species; and/or the species are likely to raise different non-prior art issues under 35 U.S.C. 101 and/or 35 U.S.C. 112, first paragraph.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species to be examined even though the requirement may be traversed (37

CFR 1.143) **and (ii) identification of the claims encompassing the elected species**, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

The election of the species may be made with or without traverse. To preserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the election of species requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected species.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the species unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other species.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim as provided by 37 CFR 1.141.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected

process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached at (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Peter J Reddig/
Examiner, Art Unit 1642

/P. J. R./